Neoadjuvant Chemotherapy and Breast Cancer

Overview

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Results: 1,523 patients 1988-1993, operable breast cancer. All patients received lumpectomy with axillary dissection or modified radical mastectomy. All patients received Tamoxifen for 5 years.

Primary object:
1. Evaluate Disease Free Survival (DFS)
2. Evaluate Overall Survival (OS)

Neoadjuvant Chemotherapy NSABP 18

Secondary Goals:
1. Evaluate clinical and pathologic response.
2. Downstage positive axillary lymph nodes
3. Convert to BCS.

Neoadjuvant Chemotherapy NSABP 18

NSABP B-18
Operable Breast Cancer

Stratification
- Age
- Clinical Tumor Size
- Clinical Node Status

Operation
AC x 4

AC x 4
Operation

Disease-Free Survival

Overall Survival

pCR
pN0
pPR
pNR
P=0.0005
P=0.0008
Neoadjuvant Chemotherapy
NSABP 18

Pathologic response is predictive of survival

<table>
<thead>
<tr>
<th></th>
<th>DFS</th>
<th>p value</th>
<th>OS</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR</td>
<td>75%</td>
<td>0.00005</td>
<td>85%</td>
<td>0.00008</td>
</tr>
<tr>
<td>pINV</td>
<td>58%</td>
<td>73%</td>
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Results are independent of age, nodal status, or tumor size.

Neoadjuvant Chemotherapy
NSABP 18

Results:
1. No difference in DFS or OS when comparing neoadjuvant to adjuvant chemotherapy.
2. For the neoadjuvant group 36% of patients had a cCR and 43% pCR for a total of 79% were downstaged. Only 3% had progression of disease.
3. Patient who had a pCR had a better DFS and OS compared to pPR. Response is predictor of prognosis, independent of receptor status, grade, and other biomarkers
4. 16% of patient downstaged the positive axillary lymph nodes.
5. Patients receiving neoadjuvant chemotherapy is more likely to have BCS. 67% vs. 60% (p=0.002)

Neoadjuvant Chemotherapy
NSABP 27

Evaluate Docetaxol in the neoadjuvant setting after 4 cycles of Adriamycin and Cytoxan

- Accrued 2,411 patients.

Primary goal:
1. Evaluate the worth of giving Docetaxol (Taxol) in the preoperative setting after 4 cycles of AC, compared to AC alone.
2. Evaluate DFS and OS
Neoadjuvant Chemotherapy
NSABP 27

Secondary goal:
1. Preoperative Docetaxol after 4 cycles of AC improve pCR, axillary nodal status, increase BCS
2. For patient who receive preoperative AC alone, did postoperative Docetaxol improve DFS and OS for patient with residual invasive cancer (pINV).

Neoadjuvant Chemotherapy
NSABP 27

NSABP B-27
Operable Breast Cancer
Randomization
AC x 4 Tam X 5 Yrs
AC x 4 Tam X 5 Yrs
AC x 4 Tam X 5 Yrs
Surgery
Docetaxel x 4
Surgery
Docetaxel x 4

NSABP 27

<table>
<thead>
<tr>
<th></th>
<th>cCR P value</th>
<th>Overall cCR+cPR P value</th>
<th>pCR P value</th>
</tr>
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<tbody>
<tr>
<td>AC&gt;T</td>
<td>65.4% 0.001</td>
<td>91.1% 0.001</td>
<td>25.6% &lt;0.001</td>
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<tr>
<td>AC</td>
<td>40.4%</td>
<td>85.7%</td>
<td>13.7%</td>
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BCS is in contrast to NSABP 18
DSF and OS data not published
Prediction for survival with biomarkers not published
Neoadjuvant Chemotherapy

- Take home points from NASBP 18 and 27
- The response to chemotherapy is predictive of DFS and OS.
- The response to chemotherapy can be used as an immediate endpoint in testing new chemotherapy or target agents.
- Evaluate biomarkers for predicting prognosis, ER, PR, grade, Ki-67, Her-2, P53, and others.
- Serial monitoring of biomarkers may provide insight into the nature and function of these markers. Example the Ki-67 or hormonal receptor status may change with neoadjuvant chemotherapy.

Evaluation of tumor response by MRI

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Post-treatment</th>
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<tbody>
<tr>
<td>Complete response</td>
<td>Complete response</td>
</tr>
<tr>
<td>Partial response</td>
<td>Partial response</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>Progressive disease</td>
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Advances in Surgical Techniques

Can Be Used After Neoadjuvant Therapy

MRI allows more accurate measure of size pre/post therapy

Pre-chemotherapy

LD=47 mm

Post-chemotherapy

LD=16 mm

(AC, 4 cycles)
Classification of Morphologic Pattern

1. Uni-centric mass with well-defined margin
2. Multi-lobulated mass with well-defined margin
3. Area enhancement with irregular margins - with nodularity
4. Area enhancement with irregular margins - without nodularity
5. Septal spread; streaming

Early Change in Tumor Volume Predictive of Final Volume Response

Neoadjuvant Chemotherapy

- Improved evaluation of mechanism of action with evaluation of treated cancer cells.
- Provide information for regarding need for additional chemotherapy (e.g., anthracyclines) or postmastectomy radiation.
- Evaluate predictors of response, Oncotype DX, Mammaprint and breast MRI.
- Downstage patients to allow BCS and lesser axillary surgery.
- Objective tumor response for high risk patients.

Neoadjuvant Chemotherapy

Consider Neoadjuvant chemotherapy for all breast cancer that are high risk for LRR and metastatic disease.

Neoadjuvant Chemotherapy

1. Breast cancers larger than 2.5 CM.
2. Triple negative breast cancers larger than 5mm
3. Her-2 positive breast cancers larger than 5mm
4. Core needle or FNA positive axillary lymph nodes.
5. Any T3 or T4 breast cancer
6. All inflammatory breast cancers.
Neoadjuvant Hormonal Therapy

Questions for future and ongoing clinical trials

1. Efficacy of neoadjuvant hormonal therapy in pre and postmenopausal women. Currently multiple trials are open using Tamoxifen, Letrozole, and Anastrozole.

2. NSABP recently opened NSABP-N-SAS-BC06

3. Alliance and CALGB recently open a DCIS trial and hormonal therapy.

4. Is surgery indicated for women who have a cCR on breast MRI. Is radiation sufficient treatment?